

Amendments to the Specification:

Please replace the paragraph beginning on page 7, line 13, with the following amended paragraph:

The present invention relates to peptides comprising an amino acid sequence substantially homologous to the amino acid sequence of a fragment of a pyrogenic exotoxin, and derivatives of said peptides, capable of eliciting protective immunity against toxic shock induced by a pyrogenic exotoxin or by a mixture of pyrogenic exotoxins.

Please replace the paragraph beginning on page 19, line 10, with the following amended paragraph:

Thus, in a first aspect, the present invention relates to peptides comprising an amino acid sequence substantially homologous to the amino acid sequence of a fragment of a pyrogenic exotoxin, and to functional derivatives of such peptides, capable of eliciting protective immunity against toxic shock induced by the exotoxins. The terms derivatives and functional derivatives used herein mean peptides with any insertions, deletions, substitutions and modifications that are capable of eliciting protective immunity against toxic shock induced by the exotoxins and/or of antagonizing toxin-mediated activation of T cells (hereafter referred to as "derivative/s").

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Please replace the paragraph beginning on page 19, line 19, with the following amended paragraph:

In a second aspect the invention relates to peptides comprising an amino acid sequence substantially homologous to the amino acid sequence of a fragment of a pyrogenic exotoxin, and to derivatives of such peptides, capable of antagonizing toxin-mediated activation of T cells. The peptides of the invention are capable of protecting against toxic shock induced by a pyrogenic exotoxin or by a mixture of pyrogenic exotoxins.

Please replace the paragraph beginning on page 21, line 5, with the following amended paragraph:

In a further embodiment the invention relates to peptides comprising the amino acid sequence shown in SEQ ID NO:4-3 (positions 152 to 161 of the sequence of the naturally occurring protein shown in SEQ ID NO:12) and to functional derivatives thereof, capable of eliciting protective immunity against toxic shock induced by at least one pyrogenic exotoxin and/or of antagonizing toxin-mediated activation of T cells. Also these peptides can be used for both immediate treatment of acute toxic shock and of the harmful effects which may be due to, for example, accidental food poisoning induced by the pyrogenic exotoxins and for conferring long-term immunity against such toxic shock.

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Please replace the paragraph beginning on page 21, line 19, with the following amended paragraph:

In addition, the invention relates to peptides comprising the amino acid sequence shown in SEQ ID NO:3-4 and to functional derivatives thereof, capable of eliciting protective immunity against toxic shock induced by at least one pyrogenic exotoxin and/or of antagonizing toxin-mediated activation of T cells. Also these peptides can be used for both immediate treatment of acute toxic shock and of the harmful effects which may be due to, for example, accidental food poisoning induced by the pyrogenic exotoxins and for conferring long-term immunity against such toxic shock.

Please replace the paragraph beginning on page 22, line 1, with the following amended paragraph:

A particular example may be a peptide having the amino acid sequence shown in SEQ ID NO:3-4 (hereinafter also referred to as p10(152-161)) and functional derivatives thereof, capable of eliciting protective immunity against toxic shock induced by a pyrogenic exotoxin or a mixture of pyrogenic exotoxins and/or of antagonizing toxin-mediated activation of T cells.

Please replace the paragraph beginning on page 24, line 19, with the following amended paragraph:

In addition the peptide may be extended by aromatic amino acid residue/s, which may be naturally occurring or synthetic amino acid residue/s. A preferred aromatic amino acid residue is tryptophan. Alternatively, the peptides can be extended at the N-terminus and/or C-terminus thereof with amino acids present in corresponding positions of the amino acid sequence of the naturally occurring pyrogenic exotoxin.

Please replace the paragraph beginning on page 37, line 18, with the following amended paragraph:

Ability to antagonize induction of IL-2 or IFN- γ gene expression was assayed by exposing PBMC populations to SEB in the presence of a 100- to 200-fold molar excess of an individual peptide. The resulting hybridization patterns for IL-2 and IFN- γ RNA are shown and quantitated in Fig. 4A. Antagonist activity is seen more clearly in Fig. 4B where extent of inhibition is plotted. Most peptides failed to inhibit SEB-mediated IL-2 mRNA induction perceptibly but pronounced antagonist activity was exhibited by peptides pSEB(150-161), pSEB(152-161), p12(150-161) and p10(152-161). Dodecapeptide p12(150-161) (SEQ ID NO:2) stands out as antagonist, inhibiting expression of IL-2 mRNA by 18-fold and that of IFN- γ mRNA by 10-fold. Peptide p10(152-161) (SEQ ID NO:34), which lacks the 2 N-terminal amino acids of p12(150-161), showed lower, yet still significant, antagonist

activity. In >5 experiments, each performed with a distinct PBMC population, SEB antagonist activity of p12(150-161) ranged from 9- to 40-fold inhibition of IL-2 gene induction. Corresponding extent of inhibition by p10(152-161) was up to 8-fold, other peptides remaining well below this value.

Please replace the paragraph beginning on page 38, line 21, with the following amended paragraph:

None of the peptides homologous to toxin domains involved in the interaction with T cell receptor and/or MHC class II molecule was able to inhibit the SEB-mediated induction of human IL-2, IFN- γ , and TNF- β genes. By contrast, the inventors have identified 12-mer p12(150-161), resembling a region well removed from these active sites which has the capacity to completely block expression of these cytokine genes upon their induction by SEB. The sequence of this potent antagonist peptide is man-made, deviating at various positions from the corresponding sequence in SEB; indeed, when a peptide with the natural SEB sequence was used, pSEB(150-161), it was less effective as antagonist. Antagonist activity decreased upon removal of 2 N-terminal amino acids. Despite its high degree of conservation, the charge of the corresponding sequence in SEA ~~it is~~ is neutral whilst that of pSEB(150-161) or of p12(150-161), is positive. Indeed, although SEB is 68%

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homologous with SEC, it shows only 27% homology with SEA

[Betley and Mekalanos, J Bacteriol 170:34 (1995)].

Please replace Table 4 on page 56, with the
following amended Table 4:

SEQ ID NO:	Alternative notation	Sequence
SEQ ID No. 1	pSEB(150-161)	T N K K K V T A Q E L D
SEQ ID No. 2	p12(150-161)	Y N K K K A T V Q E L D
SEQ ID No. 43	pSEB(152-161)	K K K A T V Q E L D K K K V T A Q E L D
SEQ ID No. 34	p10(152-161)	K K K V T A Q E L D K K K A T V Q E L D
SEQ ID No. 5	pSEBLC(150-161)	lc T N K K K V T A Q E L D
SEQ ID No. 6	p12LC(150-161)	lcY N K K K A T V Q E L D
SEQ ID No. 7	Dimer	Y N K K K A T V Q E L D Y N K K K A T V Q E L D
SEQ ID No. 8	Trimer	Y N K K K A T V Q E L D Y N K K K A T V Q E L D Y N K K K A T V Q E L D
SEQ ID No. 9	Cys-p12(150-161)	C Y N K K K A T V Q E L D C
SEQ ID No. 10	D-Ala	daY N K K K A T V Q E L Dda
SEQ ID No. 11	Ac-p12(150-161)	acY N K K K A T V Q E L Dda
SEQ ID No. 12	SEB	E S Q P D P K P D E L H K S S K F T G L M E N M K V L Y D D N H V S A I N V K S I D Q F L Y F D L I Y S I K D T K L G N Y D N V R V E F K N K D L A D K Y K D K Y V D V F G A N Y Y Y Q C Y F S K K T N D I N S H E T D K R K T C M Y G G V T E H N G N Q L D K Y R S I T V R V F E D G K N L L S F D V Q T N K K K V T A Q E L D Y L T R H Y L V K N K K L Y E F N N S P Y E T G Y I K F I E N E N S F W Y D M M P A P G D K F D Q S K Y L M M Y N D N K M V D S K D V K I E V Y L T T K K K